



NOTES

TYPE IV HYPERSENSITIVITY REACTIONS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Delayed, T cell-mediated (antibody-independent) hypersensitivity reaction
- 24–72 hour delayed nature due to stepwise sensitization-response progression
 - Antigen presentation by antigen presenting cells (APCs) → naive T-cells recognition → T-cells, macrophages migration, response

Role of CD4⁺ (helper) T cells, macrophages

- CD4⁺ (helper) T cells
 - APC displays antigen on MHC II receptor → naive CD4⁺ T cell binds MHC II via T cell receptor, CD4 coreceptor → T cell expresses CD28 → binds APC B7 → cobinding stimulates APC cytokine secretion
 - Interleukin (IL) 12 produced → T_H1 cell maturation → T_H1 secrete IL-2, IFN γ → proliferation of T_H1 response, macrophage recruitment, activation
 - IL-6, TGF-beta produced → T_H17 cell maturation → T_H17 secrete IL-17 → recruit neutrophils
- Macrophages
 - Secrete TNF-alpha, IL-1, IL-6 → promote inflammation, leaky endothelium → edema, fever; secrete lysosomal enzymes, complement, and reactive oxygen species (ROS) → tissue damage
- Pathophysiology in inflammatory bowel disease (IBD), multiple sclerosis (MS), rheumatoid arthritis (RA)

Role of CD8⁺ (AKA cytotoxic, effector, killer) T cells

- Altered host cell MHC I signal → CD8⁺ T cell receptor → activate CD8⁺ T cells

- Secrete perforins, granzymes → create membrane pores, induce cellular apoptosis
- Pathophysiology in Type I diabetes mellitus (DM), against islet cells; Hashimoto's thyroiditis, against epithelial cells; immune response to some tumor cells

Common Type IV hypersensitivity reactions

- Allergic contact dermatitis
- Mantoux test
- Diabetes mellitus type I
- Hashimoto's thyroiditis
- Multiple sclerosis
- Coeliac disease
- Giant-cell arteritis
- Postorgasmic illness syndrome
- Reactive arthritis
- GVHD
 - Transfusion-associated graft versus host disease

TYPES

Contact hypersensitivity

- Molecules covalently alter major histocompatibility complex (MHC) I receptors to neo-self antigens; nickel, urushiol (poison ivy molecule)

Chronic, delayed hypersensitivity

- Agents unusually resistant to elimination by immune system; tuberculosis (TB), leprosy, silicosis, sarcoidosis

COMPLICATIONS

- Granuloma formation in chronic, delayed-type hypersensitivity reactions
- Due to hyperactive macrophages, surrounding inflammatory reaction "walls off" offending agent (e.g. sarcoidosis, tuberculosis, silicosis)

VISIT...

LANZAROTE
Caliente.COM

SIGNS & SYMPTOMS

- Local inflammatory reaction → erythema, warmth, edema, fever
- Sequelae of organ-specific cell destruction
 - Islet cell destruction in pancreas → insulin-deficient (e.g. lethargy, seizure, coma)
- Chronic inflammation → granuloma formation → organ failure

DIAGNOSIS

OTHER DIAGNOSTICS

- Exposure history of molecule/agent at site of symptoms
- Contact hypersensitivity
 - Patch test (adhesive-mounted patches with miniscule amounts of allergen imbued in tape)
 - Evaluate in 48–96 hours for local skin reaction

- Tuberculosis
 - Tuberculin skin test (TST)/purified protein derivative (PPD) test
 - Intradermal injection of tuberculin protein → pre-sensitized T-cells react to antigen → measure induration size at 48–72 hours
 - Positive test (induration size) inversely related to TB exposure risk of individual

TREATMENT

MEDICATIONS

- Corticosteroids for inflammatory control
 - Systemic for severe, generalized reactions; otherwise, site-specific (e.g. topical for contact dermatitis; inhaled for hypersensitivity pneumonitis)

GRAFT-VERSUS-HOST DISEASE (GvHD)

osms.it/graft-versus-host-disease

PATHOLOGY & CAUSES

- Type of transplant rejection caused by immunocompetent, donor T cells reacting against recipient MHC I “foreign” antigens
 - Variable time course of symptoms
 - **Common targets:** skin, liver, intestine epithelial tissue
- Donor CD4⁺ T cell → recognize recipient MHC II as foreign → activated donor CD4⁺ T cells → cytokine release → **recipient macrophage, CD4⁺ recruitment** → **exacerbate cytokine response**
 - **Tumor necrosis factor (TNF) alpha:** possible cause of “metabolic wasting”

- Donor CD8⁺ T cell → recognize recipient MHC I as foreign → **activated CD8⁺ T cells** → **Fas, perforin-mediated cytotoxicity**
 - Majority of tissue destruction occurs via CD8⁺ T cells
- Similar graft-versus leukemia reaction (GvL) beneficial in individuals with leukemia due to ability to help eliminate recipient’s hematopoietic cancer cell line

RISK FACTORS

- Liver, bone marrow transplants (rich in lymphocytes)
- T cell immunodeficient individuals, newborns

SIGNS & SYMPTOMS

- Metabolic wasting/failure to thrive, maculopapular rash, jaundice, bloody diarrhea, hepatosplenomegaly

DIAGNOSIS

LAB RESULTS

- Histological analysis of easily biopsied tissue in individual with history of transplantation
 - Liver, skin, gastrointestinal (GI) tract; most helpful in chronic, indolent disease

OTHER DIAGNOSTICS

- Clinical presentation
 - Constellation of symptoms

TREATMENT

MEDICATIONS

- Prophylaxis (e.g. cyclosporine, methotrexate)
- Site-directed corticosteroids
 - Topical for primary skin manifestation; non-absorbable (e.g. budesonide, beclomethasone) for GI involvement

OTHER INTERVENTIONS

Prevention

- Proper donor, recipient human leukocyte antigen (HLA), MHC, minor histocompatibility (MiHA) matching; irradiation of transfused blood products

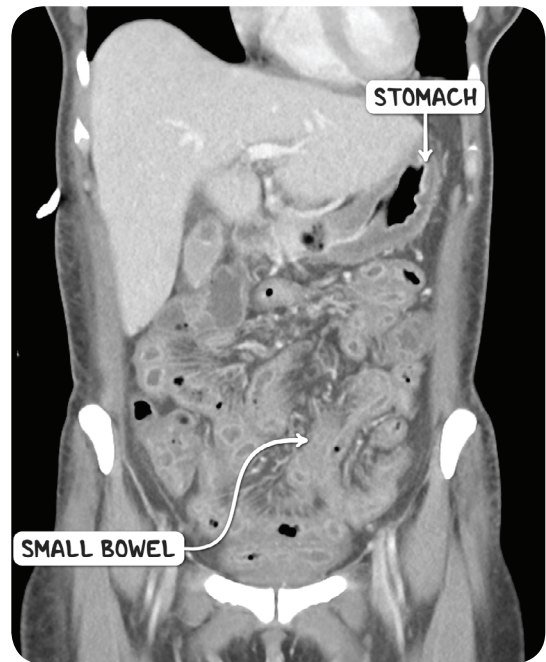


Figure 39.1 A CT scan in the coronal plane of the abdomen of an individual with graft-versus-host disease. The gastrointestinal tract, including the stomach and small bowel, is grossly edematous.

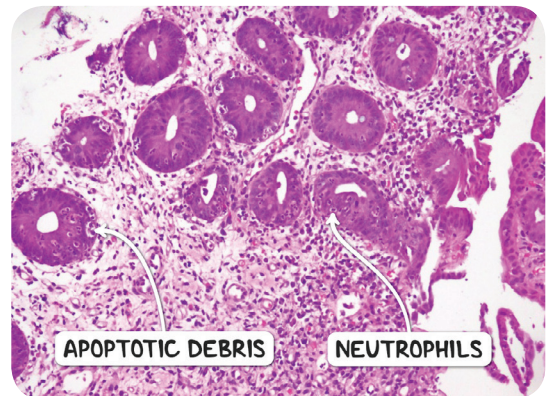


Figure 39.1 A colonic biopsy taken from an individual with graft-versus-host disease. There is florid cryptitis (neutrophils infiltrating the crypt wall) and apoptotic debris at the crypt bases.